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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,380	04/01/2002	Fabrizio Samaritani	P/42-63	7114

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EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 02/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,380	SAMARITANI ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Finality of the rejection of the last Office Action (13 January 2004) is *withdrawn* in view of the new grounds of rejection set forth below.

Status of Application, Amendments and/or Claims

The amendment filed 10 October 2003 has been entered in full. New claims 10-15 were added. Claims 1-15 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 6-10, 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maa *et al.*, US Patent No. 6,284,282 B1.

The instant claims are drawn to a pharmaceutical composition comprising a solid intimate mixture of human growth releasing factor (hGRF) and a stabilizing amount of saccharose, alone or in combination with other excipients.

Maa *et al.* teach spray freeze dry preparation (lyophilizate) of dry powder formulations of therapeutic proteins suitable for administration via pulmonary delivery. Maa *et al.* teach a method of preparing a dry powder composition comprising spray freeze-drying an aqueous mixture of a protein under conditions to provide a respirable dry powder (column 2, lines 33-44 and column 5, lines 5-29). The invention provides unit dosage receptacles and dry powder inhalers comprising a therapeutically effective amount of the dry powder composition of the invention **(claim 7)** (column 2, lines 60-64 and column 5, lines 5-29). Maa *et al.* teach that the spray freeze-dried powders of the invention comprise therapeutic proteins, including growth hormone releasing factor (hGRF) (**claim 1**)(column 6, lines 33-55). Maa *et al.* teach that the spray freeze-dried compositions may contain excipients which ensure or increase the stability of the protein during the spray freeze dry process and afterwards. Maa *et al.* lists a number of suitable excipients, including sucrose and combinations thereof (**claims 1-3, 10**)(column 8, lines 7-34). Maa *et al.* teach that the formulations, which are spray dried to form the compositions of the invention, comprise the therapeutic protein in buffer. Preferred pH

ranges of the pre-spray freeze dry formulation are from about 1 to 10 (**claims 6, 13-15**)(column 9, lines 7-27). Maa *et al.* teach that the powder compositions of the invention may be reconstituted for injection. The powder can be reconstituted into liquid form for injection (**claims 8, 9**)(column 13, line 66-column 14, line 10).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the spray freeze dry preparation of dry powder formulations of therapeutic proteins of Maa *et al.,* to make the instant invention with a reasonable expectation of success. The motivation and expected success is provided by Maa *et al.* who teach freeze-dried powders comprising hGRF and sucrose. Lastly, saccharose is also known as sucrose. The Examiner has provided a definition of saccharose from the On-line Medical Dictionary and copy of the Plant Tissue Culture Network, which list the molecular weight of sucrose (page 5, right column). The molecular weight of sucrose is the same molecular weight of saccharose as taught in the instant specification (page 4, Table 2; MW 342.30, 0.1mol=34.2).

Claims 1, 4, 5, 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maa *et al.*, US Patent No. 6,284,282 B1 as applied to claim 1 and further in view of Samaritani, WO 95/35116 (formerly cited) and Fujioka *et al.*, US Patent No. 4,963,529 (formerly cited). The teachings of Maa *et al.* are described above. Maa *et al.* do not teach do not teach pharmaceutical compositions comprising 10 mg/ vial of hGRF and 68.4 mg/vial of saccharose.

Samaritani teaches stable lyophilized pharmaceutical compositions comprising human growth hormone (hHGH) and 68.4 mg/vial of saccharose (page 1, lines 1-8 and page 6, lines 5-15). Fujioka *et al.* teach stable lyophilized pharmaceutical compositions comprising 10 mgs/vial of hGRF and human serum albumin or glycine (column 3, lines 36-55) (**claims 4, 5, 11, 12**).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the hGRF pharmaceutical composition of Maa *et al.,* by formulating it with 68.4 mg/vial of the saccharose stabilizer as taught by Samaritini and 10 mg/vial of hGRF, as taught by Fujioka *et al.*, with a reasonable expectation of success. The motivation and expected success is provided by Maa, Samaritini and Fujioka, in that Maa and Fujioka teach pharmaceutical compositions of hGRF with different stabilizers (saccharose, human serum albumin and glycine) and Samaritani teaches that highly purified proteins can be stabilized with saccharose. The adjustments of other conventional working conditions such as ranges of protein and excipient concentrations are deemed a matter of judicious selection and routine optimization, which is well within the purview of the skilled artisan. Saccharose is a known stabilizer. Maa *et al.* teach that various proteins such as growth factors, cytokines, antigens, etc, can all be stabilized with saccharose (column 6, lines 33-55).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RMD
2/7/05

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